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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
|---|---|---|---|
| 09/422,999 | 10/22/99 | KAWASAKI H | MIT-103 |

021323 HM22/0221
TESTA, HURWITZ & THIBEAULT, LLP
HIGH STREET TOWER
125 HIGH STREET
BOSTON MA 02110

| EXAMINER | |
|---|---|
| MURPHY, J | |
| **ART UNIT** | **PAPER NUMBER** |
| 1646 | 11 |

**DATE MAILED:** 02/21/01

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/422,999 | KAWASAKI ET AL. | |
| | Examiner | Art Unit | |
| | Joseph F Murphy | 1646 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *14 November 2000* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-130* is/are pending in the application.

4a) Of the above claim(s) *12-37,55-61,63-117 and 120-130* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,38-54,62 and 118-120* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

**Attachment(s)**

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7* .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☒ Other: *Sequence Comparison A* .

## DETAILED ACTION

### *Election/Restrictions*

Applicant's election of Group V, claims 1-11, 38-54, 62 and 118-120 drawn to the species SEQ ID NO: 18, in Paper No. 10 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 12-37, 55-61, 63-117 and 120-130 are withdrawn from further consideration by the Examiner as being drawn to a non-elected invention, 37 CFR 1.142(b). Claims 1-11, 38-54, 62 and 118-120 are under consideration.

### *Claim Objections*

Claims 1-11, 38-54, 62 and 118-120 are objected to because of the following informalities: They contain subject matter drawn to a non-elected invention. Appropriate correction is required.

### *Claim Rejections - 35 USC § 112 first paragraph*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4, 8-11, 38-39, 45, 48-54, 62, 118-120 are rejected under 35 U.S.C 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid encoding a polypeptide with an amino acid sequence set forth in SEQ ID NO: 18, does not reasonably provide enablement for any other nucleic acid. There is not adequate guidance as to the nature of the nucleic acid which Applicants claim. The specification does not enable any person skilled in

the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with this claim.

Claims 1-4, 8-11, 38-39, 45, 48-54, 62, 118-120 are overly broad in the recitation of "cAMP-GEFII", since no guidance as to what constitutes " cAMP-GEFII" polypeptide is provided within the claims. The broad scope of claims 1-4, 8-11, 38-39, 45, 48-54, 62, 118-120 can be read to encompass any isolated nucleic acid encoding any polypeptide. There is no guidance provided in the specification as to how one of ordinary skill in the art would generate an isolated nucleic acid encoding a polypeptide other than those exemplified in the specification. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. Given the breadth of claims 1-4, 8-11, 38-39, 45, 48-54, 62, 118-120 in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention.

Claims 38-39 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Due to the limitation of "allelic variant" and "homologue" recited in the claim, a determination of what the claim as a whole covers indicates that elements which are not particularly described, e.g. the sequence of the claimed allelic variants and homologues, are encompassed by this claim. There is no actual reduction to practice of the claimed invention, or complete detailed description of the structure. A biomolecular sequence described only by a functional characteristic, in this case an allelic variant of a nucleic acid encoding cAMP-GEF protein, without any known or disclosed correlation between the function and the structure of the sequence is not a sufficient identifying characteristic. See University of California v. Eli Lilly and Co. 43 USPQ2d at 1406. There is no known or disclosed correlation between this function and the structure of the non-described allelic variants and homologues and the disclosed isolated nucleic acid encoding a cAMP-GEF polypeptide. Weighing all factors in view of the level of knowledge and skill in the art, one skilled in the art would not recognize from the disclosure that the Applicant was in possession of the claimed invention.

Claims 50-54 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a host cell in culture comprising a nucleic acid encoding an amino acid with the sequence as set forth in SEQ ID NO: 18, does not reasonably provide enablement for in vivo transfection. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification on page 5, line 3 to page 6 line 29 discloses that the nucleic acids of the current invention can be expressed in a wide variety of host cell types, including cells within a host animal. However, there are no actual or prophetic examples that disclose how to make or use host cells that comprise a nucleic acid sequence encoding an amino acid sequence as set forth in SEQ ID NO: 18 in an animal. As is commonly known in the art, the transfection of cells within an animal with foreign nucleotide sequences is fraught with difficulty, and is complicated by many variables, including among others, the method of delivery of the polynucleotide, the appropriate vector which comprises the polynucleotide of interest, and continued expression of the polynucleotide within the host cells. The instant disclosure does not address any of the methods necessary to make a host cell in an animal which comprises the polynucleotide of interest, therefore, the claims as written are not enabled.

Claims 118-120 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification does not adequately teach how to effectively treat any disease or reach any therapeutic endpoint in humans by administering cAMP-GEF expression vectors encoding cAMP-GEF protein or cAMP-GEF antisense. See Eck & Wilson (Ref H of Paper No. 3) who report that numerous factors complicate *in vivo* gene therapy with respect to predictably achieving levels and duration of gene expression which have not been shown to be overcome by routine experimentation. These include, the fate of the DNA vector itself (volume distribution, rate of clearance into the tissues, etc.), the *in vivo* consequences of altered gene expression and protein function, the fraction of vector taken up by the target cell population, the trafficking of the genetic material within cellular organelles, the rate of degradation of the DNA, the level of mRNA produced, the stability of the mRNA produced, the amount and stability of the protein produced, and the protein's compartmentalization within the cell, or its secretory fate, once produced. See Eck and Wilson, page 82, column 1, first paragraph. These factors differ dramatically based on the protein being produced, and the disease and/or host being treated. It is further noted that Eck and Wilson supports the importance of tailoring a gene therapy vector and method to specific diseases and/or disorders and not to all diseases and disorders. See page 82, column 1, first paragraph. For example, Eck & Wilson et al. review the state of the art for gene therapy for inherited disorders and discloses that "[t]he level of protein function necessary to achieve complementation of the defect varies widely among genetic diseases." See page 78,

column 2, 2nd paragraph. As such, in light of the state of the art for gene therapy, the specification fail to provide guidance for any of the above parameters for *in vivo* gene expression nor do they provide a clear correlation to carrying out gene therapy with regard to any particular therapeutic effect with regard to any particular disease or disorder by practicing the claimed methods using the claimed nucleic acid constructs.

To this regard, MPEP section 2164 sets forth that the issue of "correlation" is also dependent on the state of the art at the time of the invention. MPEP, section 2164 goes on to discuss that if one skilled in the art cannot readily anticipate the effect of a change within the subject matter to which that claimed invention broadly pertains, then there is lack of predictability in the art. Thus, what is known in the art provides evidence as to the question of predictability.

***Claim Rejections - 35 USC § 112 second paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4, 8-11, 38-39, 45, 48-54, 62, 118-120 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-4, 8-11, 38-39, 45, 48-54, 62, 118-120 are indefinite in that they only describe the peptide of interest by an arbitrary protein name, i.e. cAMP-GEFII. There is nothing in the claims which distinctly identifies the protein. For example, others in the field may isolate the

same protein and give said protein an entirely different name. Applicant should particularly point out and distinctly identify the polypeptide by claiming structural characteristics associated with the protein (e.g. amino acid sequence, molecular weight, etc.). Identification of biochemical molecules by a particular name given to the protein by various workers in the field fails to distinctly designate what that protein is.

### *Claim Rejections - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 5-7 are rejected under 35 U.S.C. 102(b) as being anticipated by Hillier et al. (1995).

Hillier et al. discloses an isolated nucleic acid sequence which comprises at least 15 consecutive nucleic acids of SEQ ID NO: 17 (see Sequence Comparison A, Attached), thus anticipating claims 5-7.

### *Conclusion*

No claim is allowed.

***Advisory Information***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph F. Murphy whose telephone number is 703-305-7245. The examiner can normally be reached on M-F 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 703-308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
February 15, 2001

PREMA MERTZ
PRIMARY EXAMINER